15. (amended) The method of Claim 1 wherein the content of at least one member of the ceramide lipid family is increased.

16. (amended) The method of Claim 1 wherein the content of free fatty acids is increased.

29. (amended) A composition for topical administration to the skin of a mammal comprising (i) a ursolic acid compound encapsulated in liposomes and (ii) a medium suitable only for topical administration, wherein said liposomes comprise phospholipid bilayer membranes.

33. (amended) A composition for topical administration to the skin of a mammal comprising (i) a ursolic acid compound encapsulated in liposomes, (ii) at least one other therapeutically active topical compound which is not a ursolic acid compound, and (iii) a medium suitable for topical administration, wherein said liposomes comprise phospholipid bilayer membranes.

A copy of original Claims 1-4, 7, 9, 12, 15-16, 29, and 33 annotated to show the changes made by this amendment is attached as Exhibit A.

REMARKS

This is a §371 national phase filing of PCT Patent Application No. PCT/US00/24659.

To expedite the prosecution of this application, applicants have amended their claims as set forth above to more particularly define the inventive aspects of their work. Thus, independent Claim 1 has been amended to: (1) make explicit that the alteration in lipid content produced by the ursolic acid compound is an increase in lipid content, (2) require that the topical administration of the ursolic acid compound takes place with the compound encapsulated in liposomes, and (3) require that the liposomes comprise phospholipid bilayer membranes.

As a result of these changes, Claim 11 has been canceled, the dependency of Claim 12 has been changed from Claim 11 to Claim 1, and the language of Claims 15-16 has been amended to better conform to the amended language of Claim 1. In addition, the "amount effective to..." language of Claims 21-23 and

27-28 has been included in Claims 2-4, 7, and 9, with Claims 21-23 and 27-28 and their dependent Claims 24 and 25 then being canceled. Also, the claims directed to treatment of acne (i.e., Claims 8 and 26) have been canceled. Finally, Claims 29 and 33 have been amended so that like amended Claim 33, they recite that the liposomes comprise phospholipid bilayer membranes.

With these changes, all of applicants' claims include limitations calling for a ursolic acid compound encapsulated in liposomes wherein the liposomes comprise phospholipid bilayer membranes. At page 15, lines 5-11, of their specification, applicants discuss the importance of this combination as follows:

> Liposomal formulations are preferred because ursolic acid is highly insoluble in many solvents, particularly water, and common emulsifiers such as LECINOL S-10 have little effect. In accordance with the invention, this insolubility problem is addressed by taking advantage of the flat, planar structure of ursolic acid to stack it between the lipid tails in the phospholipid bilayer membranes of liposomes. Due to the charged head-group of the phospholipids, liposomes containing ursolic acid are readily soluble in water.

To applicants' knowledge, there is no disclosure or suggestion in the prior art regarding the use of liposomes to topically administer any ursolic acid compound. Likewise, the foregoing advantage of such use, namely, the solution to the solubility problem, is not disclosed or suggested in the art. Accordingly, applicants believe that their claims are both novel and nonobvious in view of the prior art and thus properly patentable.

Consideration of the foregoing in connection with the examination of this application is respectfully requested.

Respectfully submitted,

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